PATENT
ATTORNEY DOCKET NO.: 056291-5005-02

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re PATENT APPLICATION of:	)	
Andrew P. THOMAS et al.	)	Confirmation No. 2735
Application No.: 10/698,388	)	Group Art Unit: 1624
Filed: November 3, 2003	)	Examiner: Patel, S.
FOR: QUINAZOLINE DERIVATIVES AND PHARMACEUTICAL COMPOSITIONS CONTAINING THEM	)	Allowed: September 23, 2004

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Date: December 17, 2004

Sir:

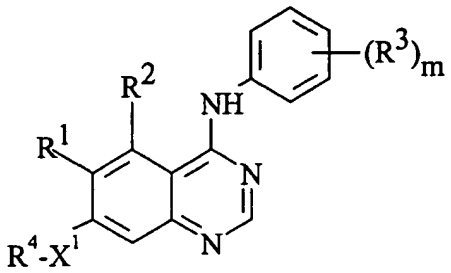
AMENDMENT UNDER 37 C.F.R. § 1.312

This Amendment under 37 C.F.R. § 1.312 is being filed to physically incorporate the structure of formula I and associated definitions from allowed method claim 17 into allowed method claims 18 and 20, in place of the reference to formula I. The amendment is for purposes of clarification, and does not, and is not intended to, change the substance or scope of claims 18 and 20. Entry of this amendment after allowance is therefore believed to be appropriate and entry thereof is respectfully requested.

IN THE CLAIMS:

Claims 1-16 (canceled).

Claim 17 (previously presented): A method for producing an anti-cancer effect in a warm-blooded animal in need of such treatment which comprises administering to said animal an effective amount of a quinazoline derivative of formula I:



(I)

wherein:

m is an integer from 1 to 2;

R^1 represents hydrogen, hydroxy, halogeno, nitro, trifluoromethyl, cyano, C_{1-3}alkyl, C_{1-3}alkoxy, C_{1-3}alkylthio, or $-NR^5R^6$ (wherein R^5 and R^6, which may be the same or different, each represents hydrogen or C_{1-3}alkyl);

R^2 represents hydrogen, hydroxy, halogeno, methoxy, amino or nitro;

R^3 represents hydroxy, halogeno, C_{1-3}alkyl, C_{1-3}alkoxy, C_{1-3}alkanoyloxy, trifluoromethyl, cyano, amino or nitro;

X^1 represents $-CH_2-$, -S-, -SO-, $-SO_2-$, $-NR^7CO-$, $-CONR^8-$, $-SO_2NR^9-$, $-NR^{10}SO_2-$ or $-NR^{11}-$ (wherein R^7, R^8, R^9, R^{10} and R^{11} each independently represents hydrogen, C_{1-3}alkyl or C_{1-3}alkoxyC_{2-3}alkyl);

R^4 is selected from one of the following twelve groups:

1) C_{1-5}alkylR^{12} (wherein R^{12} is a 5 or 6 membered saturated heterocyclic group with one or two heteroatoms, selected independently from O, S and N, which heterocyclic group is linked to C_{1-5}alkyl through a carbon atom and which heterocyclic group may bear one or two substituents selected from oxo, hydroxy, halogeno, C_{1-4}alkyl,

C_{1-4}hydroxyalkyl, C_{1-4}alkoxy, carbamoyl, C_{1-4}alkylcarbamoyl, N,N-di(C_{1-4}alkyl)carbamoyl, C_{1-4}alkanoyl and C_{1-4}alkoxycarbonyl) or C_{1-5}alkylR^{13} (wherein R^{13} is a group selected from pyrrolidin-1-yl, imidazolidin-1-yl and thiomorpholino, which group may bear one or two substituents selected from oxo, hydroxy, halogeno, C_{1-4}alkyl, C_{1-4}hydroxyalkyl, C_{1-4}alkoxy, carbamoyl, C_{1-4}alkylcarbamoyl, N,N-di(C_{1-4}alkyl)carbamoyl, C_{1-4}alkanoyl and C_{1-4}alkoxycarbonyl);

2) C_{2-5}alkenylR^{14} (wherein R^{14} is a 5 or 6 membered saturated heterocyclic group with one or two heteroatoms, selected independently from O, S and N, which heterocyclic group may bear one or two substituents selected from oxo, hydroxy, halogeno, C_{1-4}alkyl, C_{1-4}hydroxyalkyl, C_{1-4}alkoxy, carbamoyl, C_{1-4}alkylcarbamoyl, N,N-di(C_{1-4}alkyl)carbamoyl, C_{1-4}alkanoyl and C_{1-4}alkoxycarbonyl);

3) C_{2-5}alkynylR^{15} (wherein R^{15} is a 5 or 6 membered saturated heterocyclic group with one or two heteroatoms, selected independently from O, S and N, which heterocyclic group may bear one or two substituents selected from oxo, hydroxy, halogeno, C_{1-4}alkyl, C_{1-4}hydroxyalkyl, C_{1-4}alkoxy, carbamoyl, C_{1-4}alkylcarbamoyl, N,N-di(C_{1-4}alkyl)carbamoyl, C_{1-4}alkanoyl and C_{1-4}alkoxycarbonyl);

4) C_{1-5}alkylX^2C_{1-5}alkylX^3R^{16} (wherein X^2 and X^3 which may be the same or different are each -O-, -S-, -SO-, $-SO_2-$, $-NR^{17}CO-$, $-CONR^{18}-$, $-SO_2NR^{19}-$, $-NR^{20}SO_2-$ or $-NR^{21}-$ (wherein R^{17}, R^{18}, R^{19}, R^{20} and R^{21} each independently represents hydrogen, C_{1-3}alkyl or C_{1-3}alkoxyC_{2-3}alkyl) and R^{16} represents hydrogen or C_{1-3}alkyl) with the proviso that X^1 cannot be $-CH_2-$ when R^4 is C_{1-5}alkylX^2C_{1-5}alkylX^3R^{16};

5) C_{1-5}alkylX^4COR^{22} (wherein X^4 represents -O- or $-NR^{23}-$ (wherein R^{23} represents hydrogen, C_{1-3}alkyl or C_{1-3}alkoxyC_{2-3}alkyl) and R^{22} represents $-NR^{24}R^{25}$ or $-OR^{26}$ (wherein R^{24}, R^{25} and R^{26} which may be the same or different each represents hydrogen, C_{1-4}alkyl or C_{1-3}alkoxyC_{2-3}alkyl));

6) C_{1-5}alkylX^5R^{27} (wherein X^5 represents -O-, -S-, -SO-, $-SO_2-$, -OCO-, $-NR^{28}CO-$, $-CONR^{29}-$, $-SO_2NR^{30}-$, $-NR^{31}SO_2-$ or $-NR^{32}-$ (wherein R^{28}, R^{29}, R^{30}, R^{31} and R^{32} each independently represents hydrogen, C_{1-3}alkyl or C_{1-3}alkoxyC_{2-3}alkyl) or X^5 is carbonyl, and R^{27} represents cyclopentyl, cyclohexyl or a 5 or 6 membered saturated

heterocyclic group with one or two heteroatoms, selected independently from O, S and N, which cyclopentyl, cyclohexyl or heterocyclic group may bear one or two substituents selected from oxo, hydroxy, halogeno, C_{1-4}alkyl, C_{1-4}hydroxyalkyl, C_{1-4}alkoxy, carbamoyl, C_{1-4}alkylcarbamoyl, N,N-di(C_{1-4}alkyl)carbamoyl, C_{1-4}alkanoyl and C_{1-4}alkoxycarbonyl or R^{27} is C_{1-3}alkyl with the proviso that when R^{27} is C_{1-3}alkyl, X^5 is -S-, -SO-, $-SO_2-$, $-SO_2NR^{30}-$ or $-NR^{31}SO_2-$ and X^1 is not $-CH_2-$);

7) C_{1-3}alkoxyC_{2-4}alkyl provided that X^1 is -S-, -SO- or $-SO_2-$;

8) C_{1-5}alkylX^6C_{1-5}alkylR^{33} (wherein X^6 represents -O-, -S-, -SO-, $-SO_2-$, $-NR^{34}CO-$, $-CONR^{35}-$, $-SO_2NR^{36}-$, $-NR^{37}SO_2-$ or $-NR^{38}-$ (wherein R^{34}, R^{35}, R^{36}, R^{37} and R^{38} each independently represents hydrogen, C_{1-3}alkyl or C_{1-3}alkoxyC_{2-3}alkyl) and R^{33} represents cyclopentyl, cyclohexyl or a 5 or 6 membered saturated heterocyclic group with one or two heteroatoms, selected independently from O, S and N, which cyclopentyl, cyclohexyl or heterocyclic group may bear one or two substituents selected from oxo, hydroxy, halogeno, C_{1-4}alkyl, C_{1-4}hydroxyalkyl, C_{1-4}alkoxy, carbamoyl, C_{1-4}alkylcarbamoyl, N,N-di(C_{1-4}alkyl)carbamoyl, C_{1-4}alkanoyl and C_{1-4}alkoxycarbonyl);

9) R^{39} (wherein R^{39} is a group selected from pyrrolidin-3-yl, piperidin-3-yl and piperidin-4-yl which group may bear one or two substituents selected from oxo, hydroxy, halogeno, C_{1-4}alkyl, C_{1-4}hydroxyalkyl, C_{1-4}alkoxy, carbamoyl, C_{1-4}alkylcarbamoyl, N,N-di(C_{1-4}alkyl)carbamoyl, C_{1-4}alkanoyl and C_{1-4}alkoxycarbonyl);

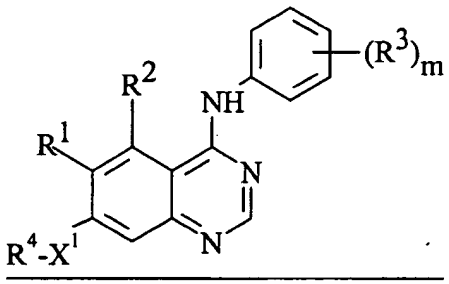
10) C_{1-5}alkylR^{40} (wherein R^{40} is piperazin-1-yl which bears at least one substituent selected from C_{1-4}alkanoyl, C_{1-4}alkoxycarbonyl, C_{1-4}hydroxyalkyl and $-CONR^{41}R^{42}$ (wherein R^{41} and R^{42} each independently represents hydrogen or C_{1-4}alkyl);

11) C_{1-5}alkylR^{43} (wherein R^{43} is morpholino which may bear one or two substituents selected from oxo, C_{1-4}alkyl, C_{1-4}hydroxyalkyl, carbamoyl, C_{1-4}alkylcarbamoyl, N,N-di(C_{1-4}alkyl)carbamoyl, C_{1-4}alkanoyl and C_{1-4}alkoxycarbonyl) with the proviso that when R^4 is C_{1-5}alkylR^{43}, X^1 is -S-, -SO-, $-SO_2-$, $-SO_2NR^9-$ or $-NR^{10}SO_2-$; and

12) C_{1-5}alkylR^{44} (wherein R^{44} is morpholino which bears at least one and optionally two substituents selected from oxo, C_{1-4}alkyl, C_{1-4}hydroxyalkyl, carbamoyl, C_{1-4}alkylcarbamoyl, N,N-di(C_{1-4}alkyl)carbamoyl, C_{1-4}alkanoyl and C_{1-4}alkoxycarbonyl);

or a pharmaceutically acceptable salt thereof.

Claim 18 (currently amended): A method for inhibiting the effects of VEGF in a warm-blooded animal in need of such treatment which comprises administering to said animal an effective inhibiting amount of a quinazoline derivative of formula I:



(I)

wherein:

m is an integer from 1 to 2;

R^1 represents hydrogen, hydroxy, halogeno, nitro, trifluoromethyl, cyano, C_{1-3}alkyl, C_{1-3}alkoxy, C_{1-3}alkylthio, or $-NR^5R^6$ (wherein R^5 and R^6, which may be the same or different, each represents hydrogen or C_{1-3}alkyl);

R^2 represents hydrogen, hydroxy, halogeno, methoxy, amino or nitro;

R^3 represents hydroxy, halogeno, C_{1-3}alkyl, C_{1-3}alkoxy, C_{1-3}alkanoyloxy, trifluoromethyl, cyano, amino or nitro;

X^1 represents $-CH_2-$, $-S-$, $-SO-$, $-SO_2-$, $-NR^7CO-$, $-CONR^8-$, $-SO_2NR^9-$, $-NR^{10}SO_2-$ or $-NR^{11}-$ (wherein R^7, R^8, R^9, R^{10} and R^{11} each independently represents hydrogen, C_{1-3}alkyl or C_{1-3}alkoxyC_{2-3}alkyl);

R^4 is selected from one of the following twelve groups:

1) C_{1-5}alkylR^{12} (wherein R^{12} is a 5 or 6 membered saturated heterocyclic group with one or two heteroatoms, selected independently from O, S and N, which heterocyclic group is linked to C_{1-5}alkyl through a carbon atom and which heterocyclic group may bear one or two substituents selected from oxo, hydroxy, halogeno, C_{1-4}alkyl, C_{1-4}hydroxyalkyl, C_{1-4}alkoxy, carbamoyl, C_{1-4}alkylcarbamoyl, N,N-di(C_{1-4}alkyl)carbamoyl, C_{1-4}alkanoyl and C_{1-4}alkoxycarbonyl) or C_{1-5}alkylR^{13} (wherein R^{13} is a group selected from pyrrolidin-1-yl, imidazolidin-1-yl and thiomorpholino, which group may bear one or two substituents selected from oxo, hydroxy, halogeno, C_{1-4}alkyl, C_{1-4}hydroxyalkyl, C_{1-4}alkoxy, carbamoyl, C_{1-4}alkylcarbamoyl, N,N-di(C_{1-4}alkyl)carbamoyl, C_{1-4}alkanoyl and C_{1-4}alkoxycarbonyl);

2) C_{2-5}alkenylR^{14} (wherein R^{14} is a 5 or 6 membered saturated heterocyclic group with one or two heteroatoms, selected independently from O, S and N, which heterocyclic group may bear one or two substituents selected from oxo, hydroxy, halogeno, C_{1-4}alkyl, C_{1-4}hydroxyalkyl, C_{1-4}alkoxy, carbamoyl, C_{1-4}alkylcarbamoyl, N,N-di(C_{1-4}alkyl)carbamoyl, C_{1-4}alkanoyl and C_{1-4}alkoxycarbonyl);

3) C_{2-5}alkynylR^{15} (wherein R^{15} is a 5 or 6 membered saturated heterocyclic group with one or two heteroatoms, selected independently from O, S and N, which heterocyclic group may bear one or two substituents selected from oxo, hydroxy, halogeno, C_{1-4}alkyl, C_{1-4}hydroxyalkyl, C_{1-4}alkoxy, carbamoyl, C_{1-4}alkylcarbamoyl, N,N-di(C_{1-4}alkyl)carbamoyl, C_{1-4}alkanoyl and C_{1-4}alkoxycarbonyl);

4) C_{1-5}alkylX^2C_{1-5}alkylX^3R^{16} (wherein X^2 and X^3 which may be the same or different are each -O-, -S-, -SO-, -SO_2-, -NR^{17}CO-, -$CONR^{18}$-, -SO_2NR^{19}-, -$NR^{20}SO_2$- or -NR^{21}- (wherein R^{17}, R^{18}, R^{19}, R^{20} and R^{21} each independently represents hydrogen, C_{1-3}alkyl or C_{1-3}alkoxyC_{2-3}alkyl) and R^{16} represents hydrogen or C_{1-3}alkyl) with the proviso that X^1 cannot be -CH_2- when R^4 is C_{1-5}alkylX^2C_{1-5}alkylX^3R^{16};

5) C_{1-5}alkylX^4COR^{22} (wherein X^4 represents -O- or -NR^{23}- (wherein R^{23} represents hydrogen, C_{1-3}alkyl or C_{1-3}alkoxyC_{2-3}alkyl) and R^{22} represents -$NR^{24}R^{25}$ or -OR^{26}

(wherein R^{24}, R^{25} and R^{26} which may be the same or different each represents hydrogen, C_{1-4}alkyl or C_{1-3}alkoxyC_{2-3}alkyl));

6) C_{1-5}alkylX^5R^{27} (wherein X^5 represents -O-, -S-, -SO-, $-SO_2-$, -OCO-, $-NR^{28}CO-$, $-CONR^{29}-$, $-SO_2NR^{30}-$, $-NR^{31}SO_2-$ or $-NR^{32}-$ (wherein R^{28}, R^{29}, R^{30}, R^{31} and R^{32} each independently represents hydrogen, C_{1-3}alkyl or C_{1-3}alkoxyC_{2-3}alkyl) or X^5 is carbonyl, and R^{27} represents cyclopentyl, cyclohexyl or a 5 or 6 membered saturated heterocyclic group with one or two heteroatoms, selected independently from O, S and N, which cyclopentyl, cyclohexyl or heterocyclic group may bear one or two substituents selected from oxo, hydroxy, halogeno, C_{1-4}alkyl, C_{1-4}hydroxyalkyl, C_{1-4}alkoxy, carbamoyl, C_{1-4}alkylcarbamoyl, N,N-di(C_{1-4}alkyl)carbamoyl, C_{1-4}alkanoyl and C_{1-4}alkoxycarbonyl or R^{27} is C_{1-3}alkyl with the proviso that when R^{27} is C_{1-3}alkyl, X^5 is -S-, -SO-, $-SO_2-$, $-SO_2NR^{30}-$ or $-NR^{31}SO_2-$ and X^1 is not $-CH_2-$);

7) C_{1-3}alkoxyC_{2-4}alkyl provided that X^1 is -S-, -SO- or $-SO_2-$;

8) C_{1-5}alkylX^6C_{1-5}alkylR^{33} (wherein X^6 represents -O-, -S-, -SO-, $-SO_2-$, $-NR^{34}CO-$, $-CONR^{35}-$, $-SO_2NR^{36}-$, $-NR^{37}SO_2-$ or $-NR^{38}-$ (wherein R^{34}, R^{35}, R^{36}, R^{37} and R^{38} each independently represents hydrogen, C_{1-3}alkyl or C_{1-3}alkoxyC_{2-3}alkyl) and R^{33} represents cyclopentyl, cyclohexyl or a 5 or 6 membered saturated heterocyclic group with one or two heteroatoms, selected independently from O, S and N, which cyclopentyl, cyclohexyl or heterocyclic group may bear one or two substituents selected from oxo, hydroxy, halogeno, C_{1-4}alkyl, C_{1-4}hydroxyalkyl, C_{1-4}alkoxy, carbamoyl, C_{1-4}alkylcarbamoyl, N,N-di(C_{1-4}alkyl)carbamoyl, C_{1-4}alkanoyl and C_{1-4}alkoxycarbonyl);

9) R^{39} (wherein R^{39} is a group selected from pyrrolidin-3-yl, piperidin-3-yl and piperidin-4-yl which group may bear one or two substituents selected from oxo, hydroxy, halogeno, C_{1-4}alkyl, C_{1-4}hydroxyalkyl, C_{1-4}alkoxy, carbamoyl, C_{1-4}alkylcarbamoyl, N,N-di(C_{1-4}alkyl)carbamoyl, C_{1-4}alkanoyl and C_{1-4}alkoxycarbonyl);

10) C_{1-5}alkylR^{40} (wherein R^{40} is piperazin-1-yl which bears at least one substituent selected from C_{1-4}alkanoyl, C_{1-4}alkoxycarbonyl, C_{1-4}hydroxyalkyl and -CONR^{41}R^{42} (wherein R^{41} and R^{42} each independently represents hydrogen or C_{1-4}alkyl);

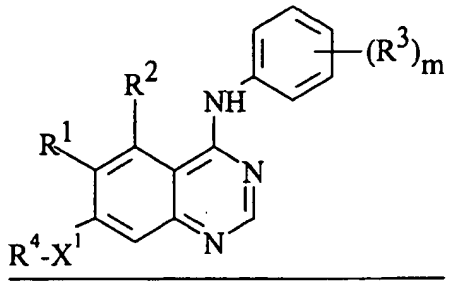
11) C_{1-5}alkylR^{43} (wherein R^{43} is morpholino which may bear one or two substituents selected from oxo, C_{1-4}alkyl, C_{1-4}hydroxyalkyl, carbamoyl, C_{1-4}alkylcarbamoyl, N,N-di(C_{1-4}alkyl)carbamoyl, C_{1-4}alkanoyl and C_{1-4}alkoxycarbonyl) with the proviso that when R^4 is C_{1-5}alkylR^{43}, X^1 is -S-, -SO-, -SO_2-, -SO_2NR^9- or -NR^{10}SO_2-; and

12) C_{1-5}alkylR^{44} (wherein R^{44} is morpholino which bears at least one and optionally two substituents selected from oxo, C_{1-4}alkyl, C_{1-4}hydroxyalkyl, carbamoyl, C_{1-4}alkylcarbamoyl, N,N-di(C_{1-4}alkyl)carbamoyl, C_{1-4}alkanoyl and C_{1-4}alkoxycarbonyl);

or a pharmaceutically acceptable salt thereof. ~~or a pharmaceutically salt thereof.~~

Claim 19 (previously presented): A method for inhibiting the effects of VEGF and EGF in a warm-blooded animal in need of such treatment which comprises administering to said animal an effective inhibiting amount of a quinazoline derivative of formula I as claimed in claim 18 or a pharmaceutically acceptable salt thereof.

Claim 20 (currently amended): A method for inhibiting the growth of a solid tumour of the colon, breast, prostate, lung or skin in a warm-blooded animal in need of such treatment which comprises administering to said animal an effective inhibiting amount of a quinazoline derivative of formula I:



(I)

wherein:

m is an integer from 1 to 2;

R^1 represents hydrogen, hydroxy, halogeno, nitro, trifluoromethyl, cyano, C_{1-3}alkyl, C_{1-3}alkoxy, C_{1-3}alkylthio, or $-NR^5R^6$ (wherein R^5 and R^6, which may be the same or different, each represents hydrogen or C_{1-3}alkyl);

R^2 represents hydrogen, hydroxy, halogeno, methoxy, amino or nitro;

R^3 represents hydroxy, halogeno, C_{1-3}alkyl, C_{1-3}alkoxy, C_{1-3}alkanoyloxy, trifluoromethyl, cyano, amino or nitro;

X^1 represents $-CH_2-$, -S-, -SO-, $-SO_2-$, $-NR^7CO-$, $-CONR^8-$, $-SO_2NR^9-$, $-NR^{10}SO_2-$ or $-NR^{11}-$ (wherein R^7, R^8, R^9, R^{10} and R^{11} each independently represents hydrogen, C_{1-3}alkyl or C_{1-3}alkoxyC_{2-3}alkyl);

R^4 is selected from one of the following twelve groups:

1) C_{1-5}alkylR^{12} (wherein R^{12} is a 5 or 6 membered saturated heterocyclic group with one or two heteroatoms, selected independently from O, S and N, which heterocyclic group is linked to C_{1-5}alkyl through a carbon atom and which heterocyclic group may bear one or two substituents selected from oxo, hydroxy, halogeno, C_{1-4}alkyl, C_{1-4}hydroxyalkyl, C_{1-4}alkoxy, carbamoyl, C_{1-4}alkylcarbamoyl, N,N-di(C_{1-4}alkyl)carbamoyl, C_{1-4}alkanoyl and C_{1-4}alkoxycarbonyl) or C_{1-5}alkylR^{13} (wherein R^{13} is a group selected from pyrrolidin-1-yl, imidazolidin-1-yl and thiomorpholino, which group may bear one or two substituents selected from oxo, hydroxy, halogeno, C_{1-4}alkyl, C_{1-4}hydroxyalkyl, C_{1-4}alkoxy, carbamoyl,

C_{1-4}alkylcarbamoyl, N,N-di(C_{1-4}alkyl)carbamoyl, C_{1-4}alkanoyl and C_{1-4}alkoxycarbonyl);

2) C_{2-5}alkenylR^{14} (wherein R^{14} is a 5 or 6 membered saturated heterocyclic group with one or two heteroatoms, selected independently from O, S and N, which heterocyclic group may bear one or two substituents selected from oxo, hydroxy, halogeno, C_{1-4}alkyl, C_{1-4}hydroxyalkyl, C_{1-4}alkoxy, carbamoyl, C_{1-4}alkylcarbamoyl, N,N-di(C_{1-4}alkyl)carbamoyl, C_{1-4}alkanoyl and C_{1-4}alkoxycarbonyl);

3) C_{2-5}alkynylR^{15} (wherein R^{15} is a 5 or 6 membered saturated heterocyclic group with one or two heteroatoms, selected independently from O, S and N, which heterocyclic group may bear one or two substituents selected from oxo, hydroxy, halogeno, C_{1-4}alkyl, C_{1-4}hydroxyalkyl, C_{1-4}alkoxy, carbamoyl, C_{1-4}alkylcarbamoyl, N,N-di(C_{1-4}alkyl)carbamoyl, C_{1-4}alkanoyl and C_{1-4}alkoxycarbonyl);

4) C_{1-5}alkylX^2C_{1-5}alkylX^3R^{16} (wherein X^2 and X^3 which may be the same or different are each -O-, -S-, -SO-, $-SO_2$-, $-NR^{17}CO$-, $-CONR^{18}$-, $-SO_2NR^{19}$-, $-NR^{20}SO_2$- or $-NR^{21}$- (wherein R^{17}, R^{18}, R^{19}, R^{20} and R^{21} each independently represents hydrogen, C_{1-3}alkyl or C_{1-3}alkoxyC_{2-3}alkyl) and R^{16} represents hydrogen or C_{1-3}alkyl) with the proviso that X^1 cannot be $-CH_2$- when R^4 is C_{1-5}alkylX^2C_{1-5}alkylX^3R^{16};

5) C_{1-5}alkylX^4COR^{22} (wherein X^4 represents -O- or $-NR^{23}$- (wherein R^{23} represents hydrogen, C_{1-3}alkyl or C_{1-3}alkoxyC_{2-3}alkyl) and R^{22} represents $-NR^{24}R^{25}$ or $-OR^{26}$ (wherein R^{24}, R^{25} and R^{26} which may be the same or different each represents hydrogen, C_{1-4}alkyl or C_{1-3}alkoxyC_{2-3}alkyl));

6) C_{1-5}alkylX^5R^{27} (wherein X^5 represents -O-, -S-, -SO-, $-SO_2$-, -OCO-, $-NR^{28}CO$-, $-CONR^{29}$-, $-SO_2NR^{30}$-, $-NR^{31}SO_2$- or $-NR^{32}$- (wherein R^{28}, R^{29}, R^{30}, R^{31} and R^{32} each independently represents hydrogen, C_{1-3}alkyl or C_{1-3}alkoxyC_{2-3}alkyl) or X^5 is carbonyl, and R^{27} represents cyclopentyl, cyclohexyl or a 5 or 6 membered saturated heterocyclic group with one or two heteroatoms, selected independently from O, S and N, which cyclopentyl, cyclohexyl or heterocyclic group may bear one or two substituents selected from oxo, hydroxy, halogeno, C_{1-4}alkyl, C_{1-4}hydroxyalkyl, C_{1-4}alkoxy, carbamoyl, C_{1-4}alkylcarbamoyl, N,N-di(C_{1-4}alkyl)carbamoyl, C_{1-4}alkanoyl and C_{1-4}alkoxycarbonyl or R^{27} is C_{1-3}alkyl with the proviso that when

R^{27} is C_{1-3}alkyl, X^5 is -S-, -SO-, $-SO_2$-, $-SO_2NR^{30}$- or $-NR^{31}SO_2$- and X^1 is not $-CH_2$-);

7) C_{1-3}alkoxyC_{2-4}alkyl provided that X^1 is -S-, -SO- or $-SO_2$-;

8) C_{1-5}alkylX^6C_{1-5}alkylR^{33} (wherein X^6 represents -O-, -S-, -SO-, $-SO_2$-, $-NR^{34}CO$-, $-CONR^{35}$-, $-SO_2NR^{36}$-, $-NR^{37}SO_2$- or $-NR^{38}$- (wherein R^{34}, R^{35}, R^{36}, R^{37} and R^{38} each independently represents hydrogen, C_{1-3}alkyl or C_{1-3}alkoxyC_{2-3}alkyl) and R^{33} represents cyclopentyl, cyclohexyl or a 5 or 6 membered saturated heterocyclic group with one or two heteroatoms, selected independently from O, S and N, which cyclopentyl, cyclohexyl or heterocyclic group may bear one or two substituents selected from oxo, hydroxy, halogeno, C_{1-4}alkyl, C_{1-4}hydroxyalkyl, C_{1-4}alkoxy, carbamoyl, C_{1-4}alkylcarbamoyl, N,N-di(C_{1-4}alkyl)carbamoyl, C_{1-4}alkanoyl and C_{1-4}alkoxycarbonyl);

9) R^{39} (wherein R^{39} is a group selected from pyrrolidin-3-yl, piperidin-3-yl and piperidin-4-yl which group may bear one or two substituents selected from oxo, hydroxy, halogeno, C_{1-4}alkyl, C_{1-4}hydroxyalkyl, C_{1-4}alkoxy, carbamoyl, C_{1-4}alkylcarbamoyl, N,N-di(C_{1-4}alkyl)carbamoyl, C_{1-4}alkanoyl and C_{1-4}alkoxycarbonyl);

10) C_{1-5}alkylR^{40} (wherein R^{40} is piperazin-1-yl which bears at least one substituent selected from C_{1-4}alkanoyl, C_{1-4}alkoxycarbonyl, C_{1-4}hydroxyalkyl and $-CONR^{41}R^{42}$ (wherein R^{41} and R^{42} each independently represents hydrogen or C_{1-4}alkyl);

11) C_{1-5}alkylR^{43} (wherein R^{43} is morpholino which may bear one or two substituents selected from oxo, C_{1-4}alkyl, C_{1-4}hydroxyalkyl, carbamoyl, C_{1-4}alkylcarbamoyl, N,N-di(C_{1-4}alkyl)carbamoyl, C_{1-4}alkanoyl and C_{1-4}alkoxycarbonyl) with the proviso that when R^4 is C_{1-5}alkylR^{43}, X^1 is -S-, -SO-, $-SO_2$-, $-SO_2NR^9$- or $-NR^{10}SO_2$-; and

12) C_{1-5}alkylR^{44} (wherein R^{44} is morpholino which bears at least one and optionally two substituents selected from oxo, C_{1-4}alkyl, C_{1-4}hydroxyalkyl, carbamoyl, C_{1-4}alkylcarbamoyl, N,N-di(C_{1-4}alkyl)carbamoyl, C_{1-4}alkanoyl and C_{1-4}alkoxycarbonyl);

or a pharmaceutically acceptable salt thereof. ~~or a pharmaceutically acceptable salt thereof.~~

Claim 21 (previously presented): The method according to claim 20 wherein the tumour is of the colon.

Claim 22 (previously presented): The method according to claim 20 wherein the tumour is of the lung.

REMARKS

Claims 18 and 20 have been amended by physically inserting therein the structure of formula I and the associated definitions taken from claim 17. On final review of these claims prior to paying the issue fee, it was noted that independent method claims 17, 18 an 20 all referred to "the quinazoline derivative of formula I," but the structure and definitions of formula I were recited only in claim 17. Therefore, for completeness of the claims, the structure of formula I and the associated definitions have been exactly copied from claim 17, and inserted in each of claims 18 and 20.

This amendment does not, and is not intended to, change the scope or substance of claims 18 and 20 in any respect and is being made for purposes of clarification and completeness. It is believed that the review and entry of this amendment does not require any significant effort on the part of the Examiner. Accordingly, it is appropriate to make this amendment after allowance, and entry of the same is respectfully requested.

EXCEPT for issue fees payable under 37 C.F.R. § 1.18, the Director is hereby authorized by this paper to charge any additional fees during the entire pendency of this application including fees due under 37 C.F.R. §§ 1.16 and 1.17 which may be required, including any required extension of time fees, or credit any overpayment to Deposit Account 50-0310. This paragraph is intended to be a **CONSTRUCTIVE PETITION FOR EXTENSION OF TIME** in accordance with 37 C.F.R. § 1.136(a)(3).

Respectfully Submitted,
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